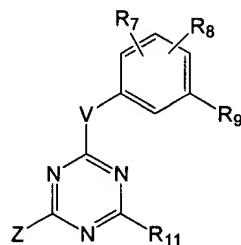


CLAIM AMENDMENTS

Below is a complete listing of all claims and replaces all prior versions.

1-65. (Canceled).

66 (Previously presented). A compound of Formula (I),



I

or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from $-\text{CHR}^5-$, $-\text{NR}^5-$, $-\text{O}-$, and $-\text{S}-$;

Z is chosen from halogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, $-\text{SR}^3$, $-\text{OR}^3$, and $-\text{N}(\text{R}^1)(\text{R}^2)$;

$-\text{N}(\text{R}^1)(\text{R}^2)$ taken together may form a heterocyclyl or substituted heterocyclyl; or

R^1 is chosen from hydrogen, alkyl and substituted alkyl; and

R^2 is chosen from alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R^3 is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R^5 is chosen from hydrogen and alkyl, or when attached to a nitrogen atom, R^5 taken together with R^7 may form a fused heterocyclyl or substituted heterocyclyl;

R^7 is chosen from hydrogen, $-\text{N}(\text{R}^{31})(\text{R}^{32})$, halogen, cyano, alkyl, substituted alkyl, alkoxy, and alkylthio, or when V is $-\text{NR}^5$, $-\text{R}^5$ and R^7 taken together may form a fused heterocyclyl or substituted heterocyclyl;

R^8 is chosen from hydrogen and halogen;

R^9 is chosen from $-\text{CO}_2(\text{alkyl})$, $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$, $-\text{SO}_2\text{N}(\text{R}^{31})(\text{R}^{32})$,

-N(R³³)SO₂R³⁴, -C(O)N(R³³)N(R³¹)(R³²), -N(R³³)C(O)R³⁴, -CH₂N(R³³)C(O)R³⁴, -N(R³¹)(R³²), -CH₂OC(O)R³⁴, C₁₋₆alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, and -C(O)R¹⁰; provided, however, that when R⁹ is CH₃ or NH₂, then neither R² nor R¹⁴ is *para*-cyano-phenyl;

or R⁸ and R⁹ taken together may form -C(O)N(R³³)CH₂- or -C(O)N(R³³)C(O)-;

R¹⁰ is chosen from heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkyl, and substituted alkyl;

R³¹ and R³³ are independently chosen from hydrogen, alkyl, and substituted alkyl;

R³² is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

R³⁴ is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R¹¹ is -N(R¹²)(R¹³);

R¹² is chosen from hydrogen, alkyl, and substituted alkyl; and

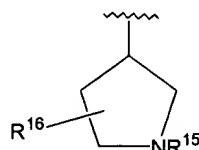
R¹³ is -(CH₂)_mR¹⁴; or

-N(R¹²)(R¹³) taken together may form a heterocyclyl or substituted heterocyclyl;

m is 0, 1, 2 or 3;

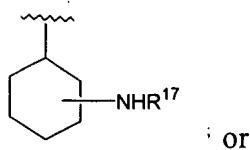
R¹⁴ is chosen from alkyl, substituted alkyl, -C(O)N(R³¹)(R³²),

-N(R³³)C(O)R³⁴, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, and



R¹⁵ is chosen from hydrogen, alkyl, substituted alkyl, alkenyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, -C(O)-substituted aryl, -C(O)-alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

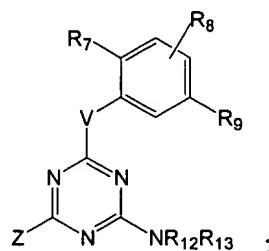
R¹⁶ is chosen hydrogen, alkyl, substituted alkyl, and



R^{17} is chosen from hydrogen, alkyl, substituted alkyl, $-C(O)$ -alkyl, $-C(O)$ -substituted alkyl, $-C(O)$ -aryl, and $-C(O)$ -substituted aryl.

67-69 (Canceled).

70. (Previously presented). A compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from $-CHR^5-$, $-NR^5-$, $-O-$, and $-S-$;

Z is halogen, alkyl, $-N(R^1)(R^2)$, or alkyl substituted with one to two of $-N(R^{31})(R^{32})$, alkoxy, alkylthio, halogen, cyano, carboxyl, hydroxyl, $-SO_2$ -alkyl, $-CO_2$ -alkyl, $-C(O)$ -alkyl, nitro, cycloalkyl, substituted cycloalkyl, $-C(O)-N(R^{31})(R^{32})$, and/or $-NH-C(O)$ -alkyl;

R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbon atoms;

R^3 is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R^5 is chosen from hydrogen and alkyl of 1 to 4 carbon atoms;

R^7 is chosen from hydrogen, amino, amino C_{1-4} alkyl, halogen, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, and alkylthio;

R^8 is attached to any available carbon atom of the phenyl ring and is chosen from hydrogen and halogen;

R^9 is chosen from $-C(O)N(R^{31})(R^{32})$, $-SO_2N(R^{31})(R^{32})$, $-N(R^{33})SO_2R^{34}$, $-C(O)N(R^{33})N(R^{31})(R^{32})$, $-N(R^{33})C(O)R^{34}$, $-CH_2N(R^{33})C(O)R^{34}$, $-N(R^{31})(R^{32})$, $-CH_2OC(O)R^{34}$, heterocyclyl, and substituted heterocyclyl; or

R^8 and R^9 taken together may form $-C(O)N(R^{33})CH_2-$ or $-C(O)N(R^{33})C(O)-$;

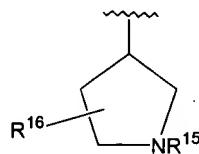
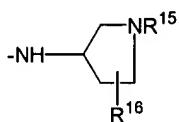
R^{31} and R^{33} are independently chosen from hydrogen, alkyl, and substituted alkyl;

R^{32} is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

R^{34} is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$-N(R^{12})(R^{13})$ taken together form (i) a monocyclic heterocyclyl or substituted heterocyclyl of 5 to 7 atoms having 1, 2 or 3 additional nitrogen atoms, (ii) $-NH$ -alkyl wherein alkyl is of 1 to 4

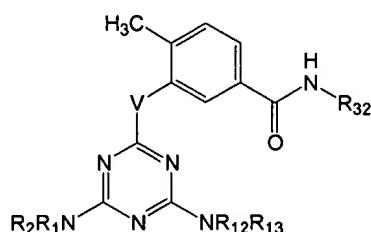
carbon atoms, or (iii)



R^{15} and R^{16} are independently hydrogen or methyl; and

R^{17} is chosen from hydrogen, alkyl, substituted alkyl, $-C(O)$ -alkyl, $-C(O)$ -substituted alkyl, $-C(O)$ -aryl, and $-C(O)$ -substituted aryl.

71 (Previously presented). A compound of Claim 70 or a enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, having the formula:



72 (Previously presented). The compound of claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof, wherein:

R^7 is halogen, methyl, methoxy, halogen, or cyano.

73 (Previously presented). The compound of claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof, wherein:

R^9 is $C(=O)NH_2$, $C(=O)NH(CH_3)$, or $C(=O)NHO(CH_3)$.

74 (Previously presented). The compound of claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof,

wherein R^7 is methyl and R^9 is $C(=O)NH(CH_3)$ or $C(=O)NHO(CH_3)$.

75 (Previously presented). A compound of Claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof wherein:

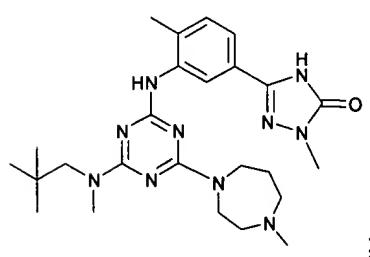
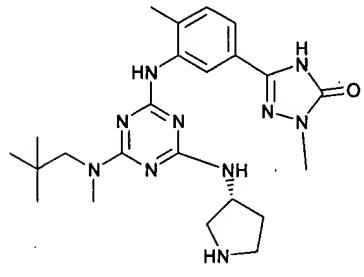
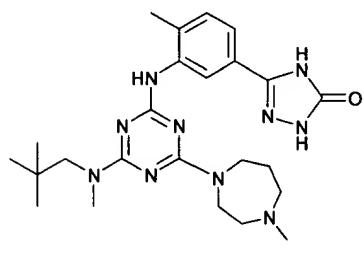
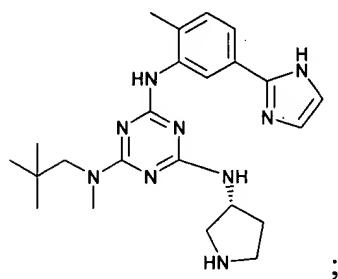
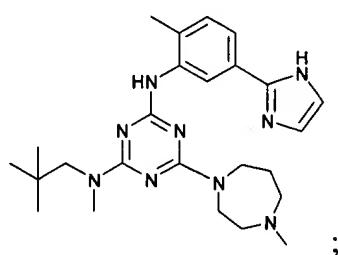
R^9 is chosen from unsubstituted or substituted triazolyl, oxadiazolyl, imidazolyl, thiazolyl and benzimidazolyl.

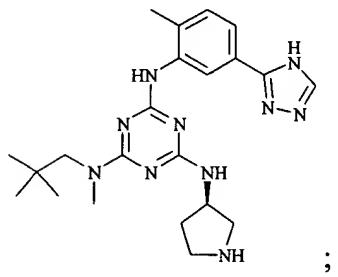
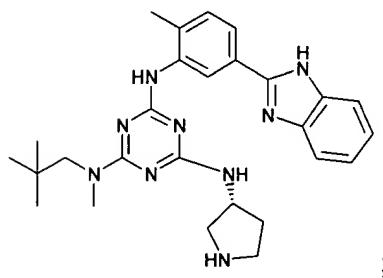
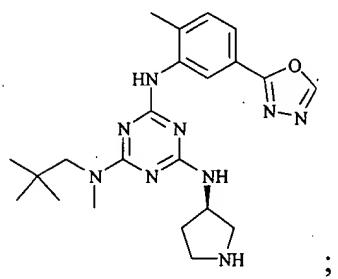
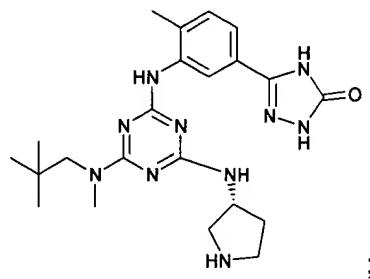
76 (Previously presented). A compound of Claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof

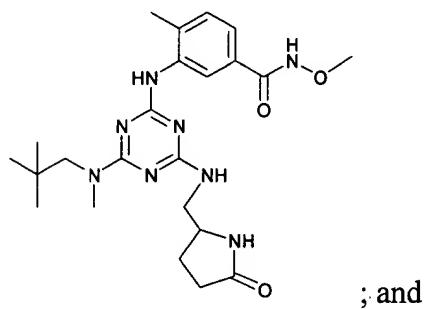
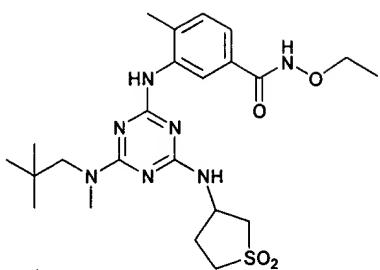
wherein:

R^9 is chosen from substituted or unsubstituted 1,2,4-triazole; substituted or unsubstituted thiazole connected via a C2, C4, or C5 position; substituted or unsubstituted 1,3,4-oxadiazole connected via a 2 or 5 position; and substituted or unsubstituted imidazole connected via a C2, C4, C5, N1 or N3 position.

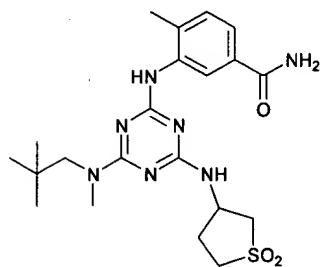
77 (Previously presented). A compound which is selected from (i):







; and

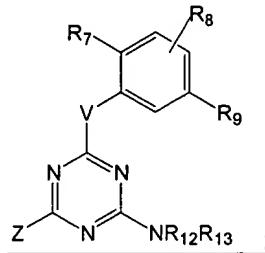


; or (ii) an enantiomer, diastereomer, tautomer, or

pharmaceutically-acceptable salt or solvate of the compound selected from paragraph (i).

78 (Previously presented). A pharmaceutical composition comprising as an active ingredient, a compound, or a salt thereof, according to claim 70, and a pharmaceutically acceptable carrier.

79 (Amended). A pharmaceutical composition according to claim 78, comprising as an active ingredient, a compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof, wherein:

V is chosen from -CHR⁵-, -NR⁵-, -O-, and -S-;

Z is halogen, alkyl, -N(R¹)(R²), or alkyl substituted with one to two of -N(R³¹)(R³²), alkoxy, alkylthio, halogen, cyano, carboxyl, hydroxyl, -SO₂-alkyl, -CO₂-alkyl, -C(O)-alkyl, nitro, cycloalkyl, substituted cycloalkyl, -C(O)-N(R³¹)(R³²), and/or -NH-C(O)-alkyl;

R¹ is hydrogen or methyl;

R² is alkyl of 1 to 8 carbon atoms;

R³ is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R⁵ is chosen from hydrogen and alkyl of 1 to 4 carbon atoms;

R⁷ is chosen from hydrogen, amino, aminoC₁₋₄alkyl, halogen, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, and alkylthio;

R⁸ is attached to any available carbon atom of the phenyl ring and is chosen from hydrogen and halogen;

R⁹ is chosen from -C(O)N(R³¹)(R³²), -SO₂N(R³¹)(R³²), -N(R³³)SO₂R³⁴, -C(O)N(R³³)N(R³¹)(R³²), -N(R³³)C(O)R³⁴, -CH₂N(R³³)C(O)R³⁴, -N(R³¹)(R³²), -CH₂OC(O)R³⁴, heterocyclyl, and substituted heterocyclyl; or

R⁸ and R⁹ taken together may form -C(O)N(R³³)CH₂- or -C(O)N(R³³)C(O)-;

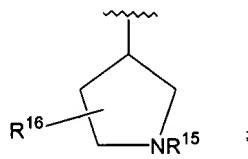
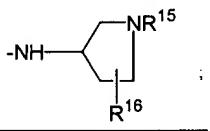
R³¹ and R³³ are independently chosen from hydrogen, alkyl, and substituted alkyl;

R³² is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

R^{34} is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$-N(R^{12})(R^{13})$ taken together form (i) a monocyclic heterocyclyl or substituted heterocyclyl of 5 to 7 atoms having 1, 2 or 3 additional nitrogen atoms, (ii) $-NH$ -alkyl wherein alkyl is of 1 to 4

carbon atoms, or (iii)



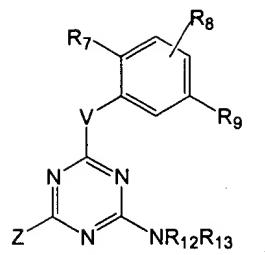
R^{15} and R^{16} are independently hydrogen or methyl; and

R^{17} is chosen from hydrogen, alkyl, substituted alkyl, $-C(O)$ -alkyl, $-C(O)$ -substituted alkyl, $-C(O)$ -aryl, and $-C(O)$ -substituted aryl and further comprising one or more additional active ingredients.

80 (Previously presented). A pharmaceutical composition according to claim 79, wherein said additional active ingredient is an anti-inflammatory compound or an immunosuppressive agent.

81 (Previously presented). A pharmaceutical composition according to claim 79, wherein said additional active ingredient is chosen from a steroid and an NSAID.

82 (Amended). A method of treating rheumatoid arthritis, the method comprising administering to a mammal an effective amount of a composition ~~according to claim 78 comprising as an active ingredient, a compound having the formula,~~



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof, wherein:

V is chosen from -CHR⁵-, -NR⁵-, -O-, and -S-;

Z is halogen, alkyl, -N(R¹)(R²), or alkyl substituted with one to two of -N(R³¹)(R³²), alkoxy, alkylthio, halogen, cyano, carboxyl, hydroxyl, -SO₂-alkyl, -CO₂-alkyl, -C(O)-alkyl, nitro, cycloalkyl, substituted cycloalkyl, -C(O)-N(R³¹)(R³²), and/or -NH-C(O)-alkyl;

R¹ is hydrogen or methyl;

R² is alkyl of 1 to 8 carbon atoms;

R³ is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R⁵ is chosen from hydrogen and alkyl of 1 to 4 carbon atoms;

R⁷ is chosen from hydrogen, amino, aminoC₁₋₄alkyl, halogen, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, and alkylthio;

R⁸ is attached to any available carbon atom of the phenyl ring and is chosen from hydrogen and halogen;

R⁹ is chosen from -C(O)N(R³¹)(R³²), -SO₂N(R³¹)(R³²), -N(R³³)SO₂R³⁴, -C(O)N(R³³)N(R³¹)(R³²), -N(R³³)C(O)R³⁴, -CH₂N(R³³)C(O)R³⁴, -N(R³¹)(R³²), -CH₂OC(O)R³⁴, heterocyclyl, and substituted heterocyclyl; or

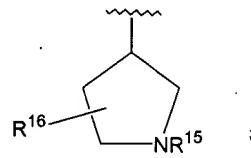
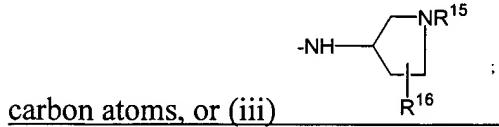
R⁸ and R⁹ taken together may form -C(O)N(R³³)CH₂- or -C(O)N(R³³)C(O)-;

R³¹ and R³³ are independently chosen from hydrogen, alkyl, and substituted alkyl;

R³² is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

R³⁴ is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$-\text{N}(\text{R}^{12})(\text{R}^{13})$ taken together form (i) a monocyclic heterocycl or substituted heterocycl of 5 to 7 atoms having 1, 2 or 3 additional nitrogen atoms, (ii) $-\text{NH-alkyl}$ wherein alkyl is of 1 to 4



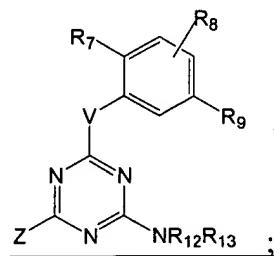
R^{15} and R^{16} are independently hydrogen or methyl; and
 R^{17} is chosen from hydrogen, alkyl, substituted alkyl, $-\text{C}(\text{O})\text{-alkyl}$,
 $-\text{C}(\text{O})\text{-substituted alkyl}$, $-\text{C}(\text{O})\text{-aryl}$, and $-\text{C}(\text{O})\text{-substituted aryl}$.

83-84 (Canceled).

85 (Amended). The method according to claim 82 wherein said composition ~~according to claim 78~~ is administered with one or more additional anti-inflammatory or immunospressive agents as a single dose form or as separate dosage forms.

86-87 (Canceled).

88 (Amended). A method of inhibiting TNF- α expression in a mammal, the method comprising administering to the mammal an effective amount of a composition ~~according to claim 78~~ comprising as an active ingredient, a compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from $-\text{CHR}^5-$, $-\text{NR}^5-$, $-\text{O}-$, and $-\text{S}-$;

Z is halogen, alkyl, $-\text{N}(\text{R}^1)(\text{R}^2)$, or alkyl substituted with one to two of $-\text{N}(\text{R}^{31})(\text{R}^{32})$, alkoxy, alkylthio, halogen, cyano, carboxyl, hydroxyl, $-\text{SO}_2$ -alkyl, $-\text{CO}_2$ -alkyl, $-\text{C}(\text{O})$ -alkyl, nitro, cycloalkyl, substituted cycloalkyl, $-\text{C}(\text{O})-\text{N}(\text{R}^{31})(\text{R}^{32})$, and/or $-\text{NH-C}(\text{O})$ -alkyl;

R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbon atoms;

R^3 is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocycl and substituted heterocycl;

R^5 is chosen from hydrogen and alkyl of 1 to 4 carbon atoms;

R^7 is chosen from hydrogen, amino, amino C_{1-4} alkyl, halogen, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, and alkylthio;

R^8 is attached to any available carbon atom of the phenyl ring and is chosen from hydrogen and halogen;

R^9 is chosen from $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$, $-\text{SO}_2\text{N}(\text{R}^{31})(\text{R}^{32})$, $-\text{N}(\text{R}^{33})\text{SO}_2\text{R}^{34}$, $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{N}(\text{R}^{31})(\text{R}^{32})$, $-\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$, $-\text{CH}_2\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$, $-\text{N}(\text{R}^{31})(\text{R}^{32})$, $-\text{CH}_2\text{OC}(\text{O})\text{R}^{34}$, heterocycl, and substituted heterocycl; or

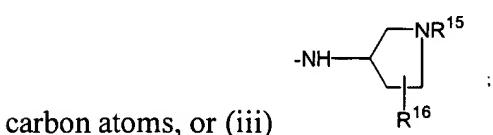
R^8 and R^9 taken together may form $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{CH}_2-$ or $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{C}(\text{O})-$;

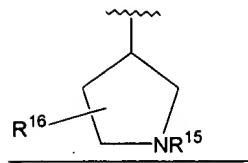
R^{31} and R^{33} are independently chosen from hydrogen, alkyl, and substituted alkyl;

R^{32} is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocycl and substituted heterocycl;

R^{34} is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocycl and substituted heterocycl;

$-\text{N}(\text{R}^{12})(\text{R}^{13})$ taken together form (i) a monocyclic heterocycl or substituted heterocycl of 5 to 7 atoms having 1, 2 or 3 additional nitrogen atoms, (ii) $-\text{NH-alkyl}$ wherein alkyl is of 1 to 4



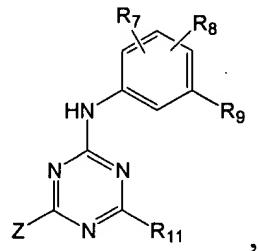


R¹⁵ and R¹⁶ are independently hydrogen or methyl; and

R¹⁷ is chosen from hydrogen, alkyl, substituted alkyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, and -C(O)-substituted aryl.

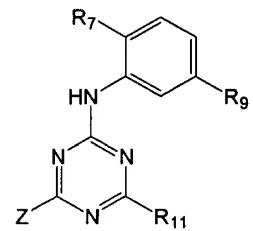
89-95 (Canceled).

96 (Previously presented). A compound according to claim 66, having the formula,



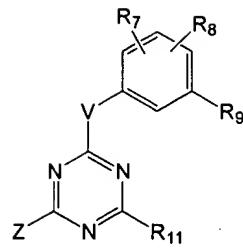
, or pharmaceutically-acceptable salt or solvate thereof.

97 (Previously presented). A compound according to claim 66, having the formula,



or pharmaceutically-acceptable salt or solvate thereof.

98 (Amended). A compound ~~according to claim 66, having the formula,~~



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or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from -CHR⁵-, -NR⁵-, -O-, and -S-;

Z is chosen from halogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, -SR³, -OR³, and -N(R¹)(R²);

-N(R¹)(R²) taken together may form a heterocyclyl or substituted heterocyclyl; or

R¹ is chosen from hydrogen, alkyl and substituted alkyl; and

R² is chosen from alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R³ is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R⁵ is chosen from hydrogen and alkyl, or when attached to a nitrogen atom, R⁵ taken together with R⁷ may form a fused heterocyclyl or substituted heterocyclyl;

R⁷ is chosen from hydrogen, -N(R³¹)(R³²), halogen, cyano, alkyl, substituted alkyl, alkoxy, and alkylthio, or when V is -NR⁵, -R⁵ and R⁷ taken together may form a fused heterocyclyl or substituted heterocyclyl;

R⁸ is chosen from hydrogen and halogen;

R⁹ is chosen from -CO₂(alkyl), -C(O)N(R³¹)(R³²), -SO₂N(R³¹)(R³²), -N(R³³)SO₂R³⁴, -C(O)N(R³³)N(R³¹)(R³²), -N(R³³)C(O)R³⁴, -CH₂N(R³³)C(O)R³⁴, -N(R³¹)(R³²), -CH₂OC(O)R³⁴, C₁₋₆alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, and -C(O)R¹⁰; provided, however, that when R⁹ is CH₃ or NH₂, then neither R² nor R¹⁴ is para-cyano-phenyl;

or R⁸ and R⁹ taken together may form -C(O)N(R³³)CH₂- or -C(O)N(R³³)C(O)-;

R¹⁰ is chosen from heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkyl, and substituted alkyl;

R³¹ and R³³ are independently chosen from hydrogen, alkyl, and substituted alkyl;

R³² is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

R³⁴ is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R¹² is chosen from hydrogen, alkyl, and substituted alkyl; and

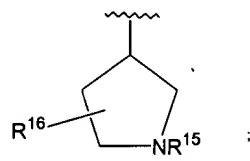
R¹³ is -(CH₂)_mR¹⁴; or

-N(R¹²)(R¹³) taken together may form a heterocyclyl or substituted heterocyclyl;

m is 0, 1, 2 or 3;

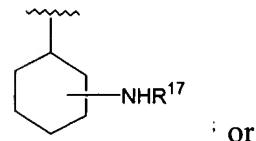
R¹⁴ is chosen from alkyl, substituted alkyl, -C(O)N(R³¹)(R³²),

-N(R³³)C(O)R³⁴, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, and



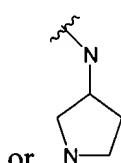
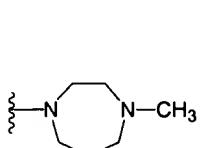
R¹⁵ is chosen from hydrogen, alkyl, substituted alkyl, alkenyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, -C(O)-substituted aryl, -C(O)-alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R¹⁶ is chosen hydrogen, alkyl, substituted alkyl, and



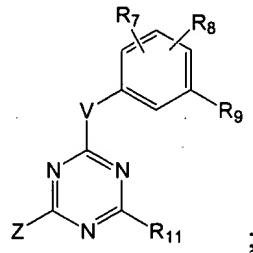
R¹⁷ is chosen from hydrogen, alkyl, substituted alkyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, and -C(O)-substituted aryl;

and wherein R₁₁ is



, or pharmaceutically-acceptable salt or solvate thereof.

99 (Previously presented). A method of modulating p38 kinase in a mammal comprising administering to the mammal at least one compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from $-\text{CHR}^5-$, $-\text{NR}^5-$, $-\text{O}-$, and $-\text{S}-$;

Z is chosen from halogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, $-\text{SR}^3$, $-\text{OR}^3$, and $-\text{N}(\text{R}^1)(\text{R}^2)$;

$-\text{N}(\text{R}^1)(\text{R}^2)$ taken together may form a heterocyclyl or substituted heterocyclyl; or

R^1 is chosen from hydrogen, alkyl and substituted alkyl; and

R^2 is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R^3 is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R^5 is chosen from hydrogen and alkyl, or when attached to a nitrogen atom, R^5 taken together with R^7 may form a fused heterocyclyl or substituted heterocyclyl;

R^7 is chosen from hydrogen, $-\text{N}(\text{R}^{31})(\text{R}^{32})$, halogen, cyano, alkyl, substituted alkyl, alkoxy, and alkylthio, or when V is $-\text{NR}^5$, $-\text{R}^5$ and R^7 taken together may form a fused heterocyclyl or substituted heterocyclyl;

R^8 is chosen from hydrogen and halogen;

R^9 is chosen from $-\text{CO}_2(\text{alkyl})$, $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$, $-\text{SO}_2\text{N}(\text{R}^{31})(\text{R}^{32})$, $-\text{N}(\text{R}^{33})\text{SO}_2\text{R}^{34}$, $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{N}(\text{R}^{31})(\text{R}^{32})$, $-\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$, $-\text{CH}_2\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$, $-\text{N}(\text{R}^{31})(\text{R}^{32})$, $-\text{CH}_2\text{OC}(\text{O})\text{R}^{34}$, $\text{C}_{1-6}\text{alkyl}$, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, and $-\text{C}(\text{O})\text{R}^{10}$; provided, however, that when R^9 is CH_3 or NH_2 , then neither R^2 nor R^{14} is *para*-cyano-phenyl;

or R⁸ and R⁹ taken together may form -C(O)N(R³³)CH₂- or -C(O)N(R³³)C(O)-;

R¹⁰ is chosen from heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkyl, and substituted alkyl;

R³¹ and R³³ are independently chosen from hydrogen, alkyl, and substituted alkyl;

R³² is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

R³⁴ is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R¹¹ is -N(R¹²)(R¹³);

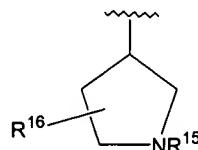
R¹² is chosen from hydrogen, alkyl, and substituted alkyl;

R¹³ is -(CH₂)_mR¹⁴;

-N(R¹²)(R¹³) taken together may form a heterocyclyl or substituted heterocyclyl;

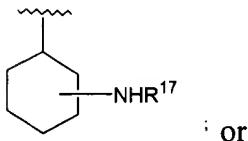
m is 0, 1, 2 or 3;

R¹⁴ is chosen from hydrogen, alkyl, substituted alkyl, -C(O)N(R³¹)(R³²), -N(R³³)C(O)R³⁴, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, and



R¹⁵ is chosen from hydrogen, alkyl, substituted alkyl, alkenyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, -C(O)-substituted aryl, -C(O)-alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R¹⁶ is chosen hydrogen, alkyl, substituted alkyl, and



R¹⁷ is chosen from hydrogen, alkyl, substituted alkyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, and -C(O)-substituted aryl.